THYROID MEDICATION IN THE TREATMENT OF DELAYED UNION OF FRACTURES.[1]

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Since the discovery of the remarkable and sometimes fatal effects of the removal of the thyroid body, much attention has been devoted to the study of the organ, and to-day we possess many interesting and practical facts concerning the important influence which the thyroid exerts on the connective tissue of the body. It is now well established that the removal, atrophy, or parenchymatous degeneration of the gland is the cause of cretinism, myxœdema, and cachexia strumipriva. Concerning the influence which the loss of function of the gland exerts on the normal development and growth of bone we are well informed. Langhans made post-mortem examinations of five cases of cretinism, all of which exhibited delay in the ossification of the epiphyseal cartilages, and in some cases in a very marked degree. He found that the bones grew very slowly in length, ossification was very slow, in the epiphyses the bony centres appeared very late, and, finally, that the epiphyseal disks are maintained far beyond the normal time, some being found as late as the forty-fifth year. A marked delay or absence of ossification in the synchondroses was also observed. In young animals, Hofmeister and Eiselberg have demonstrated that after an early thyroidectomy the development and growth of bone are affected in

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a similar manner. In cases of human cachexia strumipriva, Kocher and Reverdin have given interesting and convincing facts. The changes, therefore, in the growing skeleton due to the loss of function of the thyroid gland may be summed up as an arrest, in a high degree, of the growth of the bones in length; a material delay in the ossification of the epiphyseal cartilages and synchondroses, and, finally (according to Langhans), the presence for an abnormal length of time of a bony plate at the site of the former epiphyseal cartilage. In considering these results, one might expect that the loss of function of the thyroid would interfere with callus formation; and Steinlin has made some interesting experiments on animals to determine the influence of the thyroid on the healing of fractures. He selected young rabbits, taking two or three of the same litter; the thyroid was removed from the largest and best developed animal, and the other one or two respectively were used as control animals. As soon as the symptoms of cachexia were evident in the test animal, Steinlin fractured the inner and outer metatarsal bones of the hind feet (in some the last three ribs) of both test and control animals. These bones were chosen as they were easy to break, and did not interfere with the freedom of movement of the animal; and, besides, the inner metatarsal bones and the front ribs acting like a splint prevented too great displacement of the fractured ends. By this method a large number of fractures could be made in a single animal, and the bones thus chosen healed rapidly and are easy of microscopic examination. After a period of several weeks or months the test and control animals were killed, careful post-mortem examinations were made, and the fractured ends removed for microscopic examination. In all the test animals there was an interference of growth in general and a corresponding arrest in the development of the skeleton. The normal healing of the fractures was interfered with, in that there was not only delay in the development and absorption of the callus, but in the formation of permanent bone. During the first two weeks there was no apparent difference in both animals, but after

the third week the formation and ossification of callus were much more rapid in the control animal. At the time when bony callus was present in the control animal, calcification of the cartilaginous mass had not begun in the other, and mobility still existed at the point of fracture. In the normal animal the new medullary cavity had been formed for some time before there was inclination to formation in the trial animal, and in the latter it was not until the twenty-fourth week that the medullary cavity was formed. In all the test animals the bones finally united, there was no abolition of the healing process, and the difference was merely temporary. Steinlin's experiments were limited to a comparatively small number of young animals, and further experiments should be made, particularly on full grown animals, before we can estimate the influence which loss of the thyroid exerts on the healing of fractures. As to the effect of the thyroid on the growth of bone, a most interesting side of the question is seen in the beneficial action which thyroid medication exercises in cretinism and infantile myxœdema. Bourneville treated myxœdematous children with sheep's thyroid, and under this medication the increase in size was almost double as compared with those of normal growth.

Hertoghe asserts that the retardation of growth due to the absence of the thyroid can be corrected up to the twenty-seventh year; and he reports the case of a man, twenty-seven years of age, who gained under thyroid treatment over one and one-third inches in fourteen months.

The radiograph demonstrated incomplete ossification in the phalanges as well as the possibility of a full recovery of growth. Schmidt reports a case of myxœdema in a sixteen-year-old patient, where by means of the X-ray it was possible to see at the lower end of the femur an epiphyseal line which was clearer than the cartilaginous patella, and did not intercept the rays. Under thyroid treatment, growth was resumed and the epiphyseal line disappeared. The introduction of the X-rays has made it possible to make a continued study of the progress of bony development in infantile myxœdema and

cretinism and to appreciate the action of thyroid medication in hastening ossification.

Garne and Londe, in a nineteen-year-old patient with all the signs of myxœdema, applied the X-rays to study particularly the process of ossification, and it was found that the epiphyseal centres of the bones were like those of a child two and a half years of age. In the hand only three carpal bones were found developed. The epiphyseal centres of the metacarpal bones were scarcely visible and entirely absent in the phalanges, excepting the third phalanx of the middle and ring fingers. The patient was treated with thyroid gland in substance and consumed sixty-one glands in four months, and at the end of this time considerable progress of ossification was found. Two more carpal bones made their appearance in the skiagraph, and the metacarpals and phalanges all had developed from epiphyseal centres. As a result of these discoveries concerning the influence of the thyroid on the development of bone and the beneficial results following thyroid medication, it was proposed by Hanau, in 1896, that thyroid treatment should be used to bring about consolidation in cases of delayed union of fractures. In 1897 Gauthier reported two successful cases.

The first case was a girl fifteen years of age, who on December 29, 1896, sustained a simple fracture of the lower third of the left femur. Plaster splint applied, and when removed a month later the fragments were in good position, but there was non-union. The same condition continued up to April 15,—*i.e.*, 110 days from time of fracture—when thyroid treatment was begun. Six to ten teaspoonfuls of a glycerin extract of fresh thyroid were given daily,—each teaspoonful corresponding to a gramme of thyroid substance,—and in fourteen days signs of consolidation were evident, and on May 20 the union was complete. The patient's thyroids could be felt.

The second case was a man, forty-eight years old, who sustained on January 10, 1897, a simple fracture of the upper third of the radius. After three months no union, crepitus still present; and on April 20 thyroid treatment begun and continued to May 15 (110 grammes of thyroid gland taken in all), when

union was complete and the arm as strong as the other one. In this case the thyroid could be felt.

Quenn reports a case of compound T-shaped fracture of lower end of femur in a girl twenty-four years of age. Suppuration followed and lasted four months, when a small piece of dead bone was discharged; healing of wound rapidly ensued. At this time entire absence of bony union was present. Capsules of thyroidin were given, and in five days union had advanced to such a degree that a silicate splint was applied and the patient commenced walking with the aid of a cane; complete recovery followed. Reclus reported a case of pseudarthrosis of the femur where there was no apparent reason for delayed union. Before resorting to operation, he tried capsules of thyroidin, and in a very short time callus formed and consolidation was complete.

In another case, the result was absolutely negative; and Reclus adds that in the presence of these contradictory cases he is unable to draw any clear conclusions as to the efficiency of thyroid treatment; but he was able to report that in a case of exuberant callus thyroidin was used with excellent results. Folet reports a case of simple fracture of tibia treated in bed with splints; no union at the end of a month. Ambulatory treatment then instituted; no signs of union at end of two weeks. Thyroidin pastilles (each representing twenty centigrammes of fresh thyroid) ordered, one *t. i. d.* In ten weeks bony union was almost complete. Tronchet reports two successful cases.

The first was comminuted simple fracture of left tibia just above the ankle-joint, in a man fifty years old. Treatment was immobilization at first, then massage combined with immobilization. On the eighty-first day after fracture non-union still persisted; thyroidin tablets were then given daily, and in fifty days union was perfect. Before the thyroid treatment was resorted to, large doses of lime phosphate had been given, and the ends of the fragments rubbed together with apparently no result.

The second case was a fracture of the left tenth rib in a man fifty-six years old. On the thirty-fifth day, crepitus still present, no bony union; thyroidin tablets were given daily, and in ten days union was apparently complete.

Guinard reported a case of pseudarthrosis following fracture of tibia. He made a resection and put the limb in a plaster splint, which was removed at the end of forty days, and non-union was still present. Thyroidin was then given, but the result was a complete failure. Poirier also reports an unsuccessful result after thyroid medication in a case of delayed union of the femur. But in a case of fracture of the tibia, where at the end of three months the fragments had failed to unite, he applied a plaster splint and gave thyroidin; bony union was complete at the end of fifty days.

Rochard reports a case of pseudarthrosis of both bones of the forearm; suture of the ends of the fragments was unsuccessful, and at the end of three months thyroidin was prescribed; result absolutely negative.

In *La Scalpel,* October, 1899 (quoted by Tronchet), are reports of two successful cases. One a pseudarthrosis of the femur cured in one month; the second a fracture of the humerus with non-union at the end of two months. Both rapidly united following thyroid medication.

Ferria (quoted by Tronchet) reports two successes with thyroid treatment. The first a fracture of radius, where, owing to the deformity of the callus, the forearm remained in a position of pronation. Subperiosteal resection of callus. Three months afterwards mobility still persisted. One month of thyroid treatment was followed by complete union of the fragments. The second was a compound comminuted fracture of lower part of the tibia, where, owing to sepsis, eight centimetres of the bone were resected and replaced by a piece of the humerus. Three months later there was no union; thyroid treatment begun, and in six weeks there was a layer of new bone formed of some thickness. The interposed piece of the humerus was then removed, and some months later bony consolidation was perfect.

Steinlin's article contains two personal communications, one from Stahel, who in a case of pseudarthrosis observed no benefit from thyroid medication; the other from Kuppeler, who obtained a hastening of union in a case of delayed union.

The above cases are the result of a short review of the literature, and to them may be added the following personal observation.

A. P., laborer, twenty-eight years old, admitted to the New York Hospital August 22, 1899. Personal and family history good. Patient a small man, well developed, and in good general condition. On November 28, 1898, he was struck by a locomotive and sustained two simple fractures of the left femur,—one at the juncture of the upper and middle thirds, the other of the lower third of the bone. He was treated in a neighboring hospital, and at the end of two months there was found non-union of the upper fracture with overlapping of the fragments.

In February, 1899, the fragments were exposed, their ends freshened, and plaster splint applied to limb. In April, as non-union with deformity still existed, a resection was made and the ends united by silver-wire suture. No union followed, and in July the patient left the hospital.

When admitted to the New York Hospital, there were to be seen on the outer side of thigh the scars of the former operations; the leg and thigh were shrunken, and about one and one-half inches shortening existed. Mobility at seat of fracture was most marked, and the overlapping of the fragments could easily be felt; the lower fragment was drawn upward and behind the upper one. With the X-ray the deformity was most apparent, and there were no signs of any formation of bony callus.

On August 29, through a long incision on the outer front aspect of the thigh the ends of the fragments were exposed and freed from the fibrous tissue which united them. The ends were then caused to protrude through the wound, and after stripping back the periosteum one-fourth of an inch of bone was removed from each end. The fragments were then brought easily into coaptation, and were united by two stout silver-wire sutures. The periosteum was carefully sutured over the wires. Soft parts sutured, sterilized dressing applied, and limb put in the Buck extension apparatus. Union of soft parts was per primam. Six weeks afterwards (October 10) examinations showed that the fragments were in good position, but there was non-union. Plaster splint applied and an elixir of phosphorus pre-

scribed. On November 15 splint removed, and no change was found as regards union. Plaster splint again applied to limb, and thyroid medication was begun, the patient receiving three times a day a tablet containing two grains of the thyroid extract. On November 29 the dose was increased to three grains, and on December 7 to four grains. Examination on December 15 showed some signs of commencing union in that there was less mobility, absence of crepitude, and some thickening about the ends of the fragments. On January 2 the thickening about the ends of the bone had increased and was firmer, mobility decidedly less. Lateral plaster starts from hip to ankle applied and patient was allowed up on crutches. Thyroid extract increased to forty-five grains daily, but has since been decreased. At present there is some mobility remaining, no crepitus, and less projection of the upper fragment when patient elevates the limb.

With the X-ray, some lateral displacement of the upper fragment can be seen, and apparently is due to the cutting out of one of the silver sutures. Around the ends of the bone there is a considerable deposit of bony callus, and there is some bony union between the ends of the fragments.

The result in this case is as yet not entirely successful, but there has been gradual improvement since the beginning of the thyroid medication, and complete consolidation seems to be merely a matter of time. It was not a promising case to start with, owing to the fact of the complete failure of the previous operations, and a rapid healing was not expected. The non-union following the accident may have been due to the faulty position of the fragments, and the same reason may hold for the failure of union following the first operation. The silver-wire suture which was used in the second operation was too small and broke (as it was found broken at the time of the third operation), and thus allowed an overlapping of the fragments. When I operated, I used very stout silver wire, which has secured a good apposition of the ends of the bone, so that the non-union following this third operation was not due to faulty position of the fragments.

As to the benefit exerted by the thyroid treatment in this

case, it certainly has not been rapid; but I am inclined to give it credit, as it was not until the administration was commenced that there were any signs of progress in the healing of the fracture. The limited research I have made comprises nineteen cases, of which thirteen were reported as successful, five as failures, and my own case can be put down as improved. Although the percentage of successes is more than double that of failures, it is yet too early to form definite conclusions as to the success one may expect from the use of this treatment of delayed union of fractures. Further investigation is necessary, and a large number of cases must be observed before we can know in what class of cases we should resort to this form of treatment. Before deciding to use the thyroid, one should consider the cause of non-union in the individual case, whether it is due to some constitutional condition which may be corrected by appropriate medication, or whether there may be some local cause, which can be removed only by operation. In the absence of such causes, the thyroid treatment is indicated, and should be used in preference to resorting to any of the numerous operations which have been devised to effect union. Bearing in mind the more or less serious symptoms which may follow too large a dose, the treatment should be started with small doses. Tablets or capsules, each containing two grains of the thyroid extract, are sufficient to start with, then gradually increasing the amount every few days, and watching at the same time for any unpleasant symptoms. Overdosing may produce an effect opposite to that which we are striving for, as it has been observed in cases of infantile myxœdema that, in the presence of too large doses, while the bones steadily increase in size, they still remain soft. No unpleasant results were, as a rule, observed in the cases reported above, with the exception of Tronchet's second case, when on the eleventh day of treatment the patient had an attack of aphasia accompanied with diminution of sensibility and motion of the entire right side of the body. As the patient was a pronounced alcoholic, the attack may have been due to this cause and not as a result of the thyroid treatment.

Finally, it should not be forgotten that the heart and kidneys should be carefully examined before resorting to this form of medication, as it is contra-indicated when these organs are diseased. From the results in these cases thus far reported, and from the fact that under medical supervision the thyroid therapy is not dangerous, we are justified in recommending the trial of thyroid treatment before proceeding to operative measures.

["*May* 15.—The result of thyroid medication in the writer's case is a failure. The improvement noted in January did not continue, so the patient was admitted to my service at St. Luke's Hospital at the end of February. He was again placed in bed, a plaster splint applied to leg and thigh, and thyroid again administered. A different sample of thyroid was obtained, and was proved to be stronger than the one used at the New York Hospital. Not more than fifteen grains could be taken daily, aceton accelerating the pulse and respiration. At the end of April the splint was removed and non-union still was present. Under the X-ray there could be seen some overlapping of the fragments, and it was noted that the callus, which was present in January, has since entirely disappeared."—F. W. M.]

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